ORIGINAL ARTICLE

Cell-Assisted Lipotransfer

A Critical Appraisal of the Evidence

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SUMMARY

Background: Because of their easy accessibility and versatile biological properties, mesenchymal stem cells taken from fatty tissue (adipose-derived stem cells, ADSC) are attractive for various potential clinical uses. For example, ADSC can be added to fatty tissue before transplantation in the hope of improving the outcome of autologous lipotransfer: the modified procedure is called cell-assisted lipotransfer. The clinical use and commercial promotion of this novel stem-cell treatment (and others) are spreading rapidly, even though there is not yet any clear clinical evidence for its safety and efficacy.

Methods: In cooperation with the German Cochrane Center, we systematically searched the literature according to the PRISMA criteria. Eight major medical databases were searched. The retrieved publications were examined by two independent reviewers and assessed using objective criteria.

Results: After screening of the 3161 retrieved publications by title, abstract, and (where appropriate) full text, 78 were still considered relevant. 13 of these were reports of clinical studies; only 3 of the 13 met criteria for grade II or III evidence. The studies that were analyzed involved a total of 286 cell-assisted lipotransfer procedures with a longest follow-up time of 42 months. Oncological safety was not demonstrated.

Conclusion: The studies published to date have not shown that cell-assisted lipotransfer is generally superior to conventional autologous lipotransfer. They dealt with safety aspects inappropriately or not at all. The case of cell-assisted lipotransfer illustrates the indispensability of high-quality clinical evidence before the introduction of novel stem-cell-based treatments.

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For several decades now, the widespread introduction of clinical stem-cell therapies has been said to be just around the corner. Stem-cell research continues to be a highly dynamic field, yet there is still only one routine and widespread treatment employing stem cells, i.e., hematopoietic stem-cell transplantation (1). A number of therapeutic procedures that are claimed to exploit various properties of “stem cells” are now being promoted, sometimes aggressively, in both the scientific literature and the lay press. Increasingly, direct advertising to potential patients is being broadcast over the Internet (2–4).

Stem cells from fatty tissue (adipose-derived stem cells, ADSC) are a relatively recent member of the stem-cell family. ADSC are an adult mesenchymal stem-cell population with many advantageous features for potential clinical use. They are plentiful in human fatty tissue, and they can easily be obtained by liposuction. Their phenotypes and functions closely resemble those of stem cells from bone marrow. They have been shown to be able to differentiate into many different types of cells, including chondro-, osteo-, adipo-, myo-, and neurogenic lines, as well as endothelial cells (5). Their accessibility and versatility make them appealing not only to researchers and clinicians designing new treatments, but also to physicians who see in them a lucrative opportunity in the growing market for cosmetic treatments.

The basic elements of autologous lipotransfer were developed more than a century ago: fatty tissue is removed by excision or suction, purified, and immediately reimplanted into the same patient (6). Over the years, the technique has seen many improvements, mostly with the goal of lessening the invasiveness of cell harvesting and processing, or else simplifying and standardizing the process of reimplantation. Conventional autologous lipotransfer now consists of aspiration lipectomy with low suction, followed by purification steps and then by cell concentration by either flotation or centrifugation; finally, the purified fatty tissue is reimplanted for soft-tissue augmentation (*Figure 1*).

Typical applications of autologous lipotransfer include the correction of contour deficits after cancer surgery or radiotherapy; purely esthetic procedures (mainly on the breasts); and the treatment of facial

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FIGURE 1

Conventional compared to cell-assisted autologous lipotransfer: In the former, extracorporeal processing is limited to cleansing, concentrating, and apportioning steps that precede retransplantation of the lipograft into the target tissue by injection. In the latter, there is a major change of the cellular composition of the graft: in additional working steps in the same procedure, half of the lipoaspirate undergoes enzymatic digestion and centrifugation to isolate the “regenerative cells,” which are then added to the other half. These cells are said to account for the (putative) advantages of cell-assisted over conventional lipotransfer

atrophy due to HIV and antiretroviral drugs, systemic lupus erythematosus, or scleroderma. The limitations of this technique arise from the need for revascularization of the transplanted cells, which restricts the tissue volume that can be transplanted at once. The transplantation of an excessive volume of tissue is likely to be followed by adipocyte necrosis, volume loss, and oil cyst formation (7). Loss of transplant volume over the long term has been reported to be between 30% and 70%, even with small transplants (7, 8).

Both in vitro and in vivo experiments have yielded findings suggesting a supportive effect of ADSC on the surrounding cells in autologous lipotransfer. This has prompted the development of cell-assisted lipotransfer as a putative means of improving the outcome of transplantation. The aspirated fatty tissue is divided into two aliquots, and the ADSC-containing stromal vascular fraction is then isolated from one of the aliquots and added to the other one (Figure 1). The mixture of cells generated by this process is called the cell-enriched lipoaspirate (9).

Commercial systems for processing lipografts have been developed to make cell-assisted lipotransfer possible in a single operative sitting. These systems enable the rapid, automated generation of a cell-enriched lipoaspirate. Part of the aspirated fatty tissue is broken up and freed from the surrounding tissue matrix by application of a mixture of proteolytic enzymes; this tissue is then washed, and “regenerative cells” are removed from it by centrifugation and added to the rest of the aspirated fatty tissue to make the cell-enriched lipoaspirate (10, 11).

The cell-enriched lipoaspirate can be reimplanted anywhere in the body, depending on the indication. The most common indications at present are esthetic breast augmentation and breast reconstruction after tumor surgery (12).

The rationale behind cell-assisted lipotransfer lies in the hope that the higher concentration of ADSCs in the cell-enriched lipoaspirate, compared to the lipoaspirate of conventional autologous lipotransfer, will enable better vascularization of the graft, thereby lessening the likelihood of necrosis and adipocyte resorption, and in the hope that the transplanted ADSC will differentiate into mature adipocytes (13). If these things happen, one should be able to transplant much larger volumes of fatty tissue at one time; in the future, one might even be able to transplant autologous fatty tissue in cases where silicon breast implants are used now. This would be a veritable revolution in reconstructive and esthetic surgery, yielding major benefits of various kinds—not least financial.

There have been some encouraging findings from basic research, but hardly any clinical data on cell-assisted lipotransfer are available to date. Nor is anything known about safety issues such as the risk of inappropriate tissue differentiation or of neoplasia, an inherent danger of any stem-cell-based treatment (14, 15). The practitioners of cell-assisted lipotransfer are becoming more numerous, the advertising promoting it more intense; nonetheless, there are still no reliable figures on the frequency with which this technique is performed (Paul Ehrlich Institute, personal communications).

This state of affairs prompted us to examine the available evidence for the promising, yet controversial technique of cell-assisted lipotransfer. In accordance with the PRISMA Statement (16), we asked the following question, to be answered by application of the PICO criteria (participants, intervention, comparison, outcome): “What evidence can be found in the current scientific literature about the clinical use of fatty tissue enriched with ADSC for the purpose of regeneration and augmentation of the soft tissues?”

Methods

We conducted a systematic review of the literature in collaboration with the German Cochrane Center. A dedicated search strategy was developed with the aim of optimally representing the state of the evidence. Eight major scientific databases were searched: Medline, Medline in Process, Web of Science, BIOSIS, Scopus, LILACS, the Cochrane Library, as well as the relevant databases for registered clinical trials, including ClinicalTrials.gov, ISRCTN, the German Clinical Trials Register (DRKS), the EU Clinical Trials Register, and the Japan Primary Registries Network. The search algorithm (described in detail in the *eSupplement*) was adapted to the syntax of each database. After the initial run of the search algorithm, the data were continually and automatically updated (*Figure 2*).

Results

The search yielded 3161 hits, not including duplicates; independent screening of their titles and abstracts by two independent reviewers (SG and FL), as required by the “four-eyes principle,” yielded 228 that were judged to be potentially relevant. 78 were still considered relevant when their full text had been read, two of which turned out to be different language versions of the same content. Only 10 (13%) contained primary data (9, 12, 14, 17–22, [Asano Y, Yoshimura K: Cell-assisted lipotransfer for breast reconstruction after breast conserving therapy. *EJC Supplements* 2010; 8: 3.]). Of the remaining 67 publications, 50 were reviews, only two of which were acceptable as systematic reviews by current standards (23–25). The rest consisted of letters to the editor, editorials, comments, expert opinion, discussion contributions, book abstracts, and a company profile. Three further studies were identified by the updating system and will be discussed separately below (11, 26, 27).

The studies were too heterogeneous for meta-analysis and were therefore all analyzed as recommended in the PRISMA Statement to assure reproducible comparability and categorization (16). Each study was assigned an evidence level according to the Oxford Classification Criteria of 2011 (28).

The commonest inclusion criteria for the analyzed studies were breast reconstruction and augmentation, followed by congenital, traumatic, iatrogenic, and disease-related soft-tissue defects, facial atrophy in Parry-Romberg syndrome or systemic lupus

Search history following the PRISMA criteria. Modified from (16)

erythematosus, pectus excavatum, facial dermatofibroses, and radiation-induced soft-tissue damage (12).

Patients were typically followed up for 6 to 12 months, with the evaluation of outcomes generally based on subjective volume estimation and descriptive reports of clinical examinations, or else on photographs and videoclips. In the few studies that employed objective evaluative methods (mammography, CT/MRI volumetry), these methods often did not generate any consistent quantitative data.

Only three studies yielded grade II or III evidence; the rest yielded grade IV or V evidence. An overview of the retrieved studies is provided in the *Table*.

The reported undesired events included the formation of oil cysts, microcalcifications, fibroses, and indurations. In one case, a 17-year-old girl developed recurrent osteosarcoma after a recurrence-free interval of 10 years, 18 months after undergoing fat transplantation to the arm (14).

The 13 clinical studies involved a total of 286 cell-assisted lipotransfer procedures. The longest follow-up duration was 42 months. Adequate data on oncological safety are not available. This is especially important in view of the fact that many of these procedures were carried out at a site of prior tumor resection, e.g., for reconstruction of the breast after breast cancer surgery.

We will now discuss the three studies identified by the update system in greater detail to illustrate the sparse state of the evidence that we found.

RESTORE-2 was a one-armed, prospective, multicenter trial carried out in 2012 on 71 women with breast contour defects after breast-conserving treatment for cancer (11). Its defined primary endpoints were patient satisfaction and physician satisfaction with the functional and cosmetic outcomes of cell-assisted lipotransfer, and improvement of the pre-procedural breast deformity 12 months after the procedure. Notably, the authors had originally intended to analyze the results by MRI volumetry but could not do so, because a volume defect was demonstrable before lipotransfer in only 51 of the patients. They therefore introduced a subjective scar rating scale while the trial was in progress. This scale also "did not adequately reflect the clinical improvements," yet the authors reported that they had found a statistically significant improvement, without any further explanation of this statement. The patients' quality of life during treatment was reported to be "stable," and 45 of the 67 patients rated their satisfaction from 4 to 6 on a six-point scale, i.e., no explicit dissatisfaction was mentioned. A far more worrisome flaw of this trial was the fact that oncological safety was not addressed at all, let alone defined as an outcome parameter.

Having followed their patients up for only one year, the authors concluded that "RESTORE-2 has sufficiently demonstrated the safety and efficacy of ADRC-enriched fat grafting in the treatment of soft tissue defects post-BCT" and "this procedure should be considered as an alternative reconstructive option for women with post-BCT defects." Considering that one patient developed a distant osseous metastasis during follow-up, it seems premature at best to draw this conclusion from the RESTORE-2 trial, which was financed by the manufacturer of the device used in it (29).

In contrast, the trial of Tanikawa et al. (26) shows that high-quality research in this field is, in fact, possible. It is one of only two trials in which cell-assisted lipotransfer was studied with appropriate methodological prudence. This prospective, randomized, controlled, double-blind trial compared cell-assisted and conventional lipotransfer for the treatment of facial soft-tissue defects due to craniofacial microsomia. Despite certain limitations, including a high dropout rate and the small volumes of tissue transplanted in comparison to the amounts that are commonly transplanted in cell-assisted lipotransfer, the authors were able to show that the technique yielded better volume consistency than conventional lipotransfer for this special indication.

Peltoniemi et al. (27) arrived at the opposite conclusion in their prospective, comparative trial of autologous lipotransfer with and without "stem-cell" supplementation for esthetic breast augmentation. In the 18 women who participated in the trial, graft

survival was monitored with MRI volumetry, and the percentage of vital cells was analyzed intraoperatively with flow cytometry. Volume retention was slightly lower in the cell-assisted lipotransfer group (50% vs. 54%), but this difference was not statistically significant. The methods of this trial were generally of high quality; its limitations included a short follow-up duration (12 months at most) and a low number of patients because of the early termination of the trial for ethical reasons. The authors concluded that the transplantation of fatty tissue without any added material is "faster [and] cheaper, has a lower risk of contamination, and offers at least an equal take rate." They stated, "We do not see any advantage in stem-cell enrichment."

Discussion and conclusion

In summary, despite repeated assurances in recent years that good clinical data would soon be available, there is still no reliable evidence indicating the general superiority of cell-assisted lipotransfer over conventional lipotransfer. The single piece of evidence that favors cell-assisted lipotransfer in any way (in the report of Tanikawa et al., as discussed above) is uninformative concerning the postulated main advantage of the procedure, namely, the long-term volume retention of large grafts. Moreover, safety aspects have often been either inadequately addressed or entirely ignored. Considering that stem cells resemble tumor cells in many ways and their differentiation strongly depends on the local microenvironment, we can only conclude that, from the point of view of safety, cell-assisted lipotransfer cannot simply be considered the equivalent of conventional autologous lipotransfer.

The treatment of disease and the quest for beauty are two strong human desires to which advertisements for "stem-cell treatments" loudly and repeatedly appeal. This is not justified at present.

The fact that the materials needed to perform cell-assisted lipotransfer are generally classified as medical devices rather than pharmaceutical products, has made it easier for this technique to be adopted in routine clinical use, because the requirements for government approval of medical products are much less stringent in most countries. This could change in the future if materials for cell-assisted lipotransfer are classified as Advanced Therapy Medical Products (ATMP) in the European Union. This classification would not only be highly significant for patient safety; it would also give each treating physician special personal responsibility for complications, because the law would then consider the physician to be the manufacturer of a cellular therapeutic agent.

The initial, euphoric phase of stem-cell research is already over, but the field remains one of more innovative and promising areas in all of medicine. Clinical applications must keep pace with basic research and should not outstrip it, as has apparently occurred in the case of cell-assisted lipotransfer.

TABLE 1a

The current state of the evidence regarding cell-assisted lipotransfer

Study (source)	Indication, design, and methods	Results and conclusion	Do the findings support the conclusion?	EL	Conflict of interest?
Yoshimura 2008 (9)	Case series; 40 women who underwent CAL for esthetic breast augmentation Method: Measurement of breast size Follow-up: Up to 42 months	Estimated volume increase of 100–200 mL, stable after 2–3 months; cyst and microcalcification formation in 2 patients each	The stated superiority of CAL cannot be inferred from the study findings because of the lack of objective measurements and the lack of a control group	IV	Not stated
Tiryaki 2011(12)	Case series; CAL for volume augmentation, mainly of the breast, in 29 patients. Methods: Clinical examination, photography Follow-up: Up to 36 months	Good subjective results, possible superiority of CAL	No objective measurements, no control group, no conclusion possible	IV	No
Perrot 2010(14)	Case report of recurrent osteosarcoma in a 17-year-old female patient 18 months after threefold AFT. In vivo and in vitro investigation of potential proliferation-promoting effect of MSC on tumor cells	Recurrent sarcoma at the transplant site 18 months after AFT, after a 13-year recurrence-free interval. AFT may promote tumor recurrence, and MSC may play a role in this process.	The conclusion is reasonable but uncertain, as this is only a report of a single case	IV–V	No
Kamakura 2011(17)	Case series: Breast augmentation in 20 women Methods: Measurement of breast size, MRI (19 patients), ultraasonography, patient and physician satisfaction Follow-up: 9 months	Mean increase of breast circumference 9 months after procedure: 3.3 cm (16 patients); patients and physicians generally satisfied with outcome; no report of MRI/ultrasound findings; cyst formation in 2 women. CAL said to be effective, safe, and reliable.	The authors' conclusion is not supported by their findings; major methodological flaws	IV	Study funded by device manufacturer
Yoshimura 2008 (20)	Case report of 2 patients who received SVF sequentially after AFT; comparison with a further 146 CAL patients Methods: Clinical examination and CT Follow-up: 12 months postoperatively	Subcutaneous fibrosis 3 months after procedure; risk of maldifferentiation discussed	The conclusion is reasonable but uncertain, as the report concerns only two cases; the comparison group of 146 CAL patients is not found in any of the authors' other publications	V	No information
Rigotti 2007(18)	Case series; CAL for the treatment of radiation-induced soft-tissue defects in 20 patients Methods: Clinical examination, LENT-SOMA scale Follow-up: 30 months	"Dramatic improvement" in 19 patients; the authors state that they consider CAL the treatment of choice for radiation-induced soft-tissue injury	No criteria are given for the application of the LENT-SOMA scale; the results cannot be clearly understood; there is no control group. This study does not support the efficacy of CAL	IV	No
Asano 2010*	Case series; CAL to treat breast contour deficits after breast-conserving treatment in 26 women Method: Clinical assessment Follow-up: No information	Mainly good or very good clinical results; CAL beneficial and effective for the treatment of breast contour defects after breast-conserving treatment	Conference abstract without concrete information about study design and criteria of assessment; no control group; conclusion not supported by findings	IV–V	No information
Yoshimura 2008 (22)	Prospective, two-armed, non-randomized, partially blinded trial; CAL vs. AFT for facial lipoatrophy in 3 patients each Method: Volume estimation on photography Follow-up: 9–13 months	Clinical improvement in all patients, no statistically significant differences. 1 patient with fat necrosis. Authors' conclusion: CAL is safe, effective, and possibly superior to AFT	The postulated safety and superiority of CAL are not supported by the findings	IV	No
Yoshimura 2010(21)	Case series; CAL for breast augmentation after implant removal in 15 women Methods: Clinical examination, photography, video, mammography, MRI, 3D measurements Follow-up: Up to 18 months	Graft survival rate 40–80% by 3D measurement; high dropout rate (9/15 patients in 12 months). CAL is a possible alternative to silicone implants for breast augmentation	Conclusion basically reasonable despite high dropout-rate, variable results, and absence of a control group	IV	No information
Sterodimas 2011 (19)	Prospective, two-armed randomized trial; CAL vs. AFT in 20 patients with congenital or acquired facial soft-tissue defects. Method: Evaluation of patient satisfaction on 5-point scale. Follow-up: Up to 18 months	No significant difference in patient satisfaction at 18 months; reoperation needed in 7 patients (AFT group) versus 0 patients (CAL group)	The conclusion is reasonable, but the patient groups were small	III	No

AFT, autologous fat transfer; CAL, cell-assisted lipotransfer; EL, evidence level; LENT-SOMA, late effects on normal tissues, subjective/objective management analysis (interdisciplinary assessment of long-term oncologic treatment outcomes); MSC, mesenchymal stem cells

*Asano Y, Yoshimura K: Cell-assisted lipotransfer for breast reconstruction after breast conserving therapy. EJC Supplements 2010; 8: 3.

TABLE 1b

Further studies found by the updating process

Study	Indications, design, and methods	Results and conclusions	Do the findings support the conclusion?	EL	Conflict of interest?
Tanikawa 2013 (26)	Prospective, two-armed, randomized, blinded trial; CAL vs. AFT in 18 patients with craniofacial microsomia Method: CT volumetry Follow-up: Up to 12 months	Significantly better volume retention in the CAL group; 4 dropouts (2 per group); CAL is safe, effective, and superior to AFT	High methodological quality; sole study known to us showing an advantage for CAL for a special indication. Conclusion about safety not supported by findings. Limitations: low number of patients, high dropout rate, not generalizable to common indications	II–III	No financial conflict of interest
Perez-Cano 2012 (11)	Prospective, one-armed, multi-center trial: CAL in 71 women after breast-conserving treatment Methods: Clinical examination, LENT-SOMA, assessment of pt. satisfaction on a 6-point scale, MRI Follow-up: Up to 12 Monate	4 dropouts, repeat procedures in 24 pts., MRI abandoned for inadequate sensitivity; pts. and physicians generally satisfied; bone metastasis (1 pt.), cyst formation (10 pts.); CAL is safe and effective	Conclusion not at all supported by findings; marked methodological deficiencies	IV	Technical and financial support of the device manufacturer
Peltoniemi 2013 (27)	Prospective, two-armed, non-randomized trial; 18 patients underwent CAL or AFT for breast augmentation Method: MRI volumetry Follow-up: Up to 6 months	No significant intergroup difference; one case of cyst formation in each group; trial terminated because of lack of advantage from CAL; AFT quicker, cheaper, and theoretically safer with at least equivalent outcomes	The conclusion is reasonable, although the trial groups were small	III	No conflict of interest

AFT, autologous fat transfer; CAL, cell-assisted lipotransfer; EL, evidence level; LENT-SOMA, late effects on normal tissues, subjective/objective management analysis (interdisciplinary assessment of long-term oncologic treatment outcomes); MSC, mesenchymal stem cells; pt./pts., patient(s)

This technique is clearly a promising addition to the armamentarium of reconstructive and esthetic medicine, yet good evidence for its safety and efficacy is still lacking, and the legal framework for it remains unclear.

The claim that the transplantation of “cell-enriched” autologous fat is an “established stem-cell therapy” with the same safety profile as conventional autologous lipotransfer deviates from the standards of good clinical practice and should not be perpetuated. We strongly advise against the performance of these or similar procedures except under the rigorous conditions of clinical trials (which are urgently needed), in close collaboration with the responsible authorities, until sufficient clinical data are available to permit an assessment of the safety and efficacy of the technique. In order to answer the critical question of oncological long-term safety we consider the introduction of clinical registries indispensable.

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Conflict of interest statement

The authors state that they have no conflicts of interest.

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KEY MESSAGES

- Fatty tissue is a plentiful and easily accessible source of mesenchymal stem cells (adipose-derived stem cells, ADSC), which have attractive properties for a multitude of clinical uses.
- As a result, so-called “cell-assisted lipotransfer” (CAL) is being aggressively promoted as a way to improve the outcome of autologous lipotransfer for soft-tissue augmentation. In this method, the lipograft is enriched with ADSC.
- The goal of the present study is to assess the state of the evidence for this promising but controversial treatment with a systematic literature review.
- The currently available clinical data do not show the general superiority of cell-assisted lipotransfer over conventional treatments for soft-tissue defects, nor has the oncologic safety of the technique been demonstrated.
- Having reviewed all the available data, we view the current promotion and use of this technique for esthetic and reconstructive indications as a premature transfer of scientific findings from the bench to the bedside.
- As with other currently popular “stem-cell therapies,” the clinical use of this technique seems highly questionable or even dangerous, except in well-designed clinical trials.

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eSUPPLEMENT

Database(s): Ovid MEDLINE(R) search strategies

- 1 ((adipos* adj6 stem adj6 cell*) or (adipoc* adj6 stem adj6 cell*)).mp.
- 2 ((adipos* adj6 progenitor* adj6 cell*) or (adipoc* adj6 progenitor* adj6 cell*)).mp.
- 3 (ASCs or ADSC* or ADRC* or (ASC and adipo*)).ti,ab.
- 4 (preadipocyt* or pre-adipocyt*).ti,ab.
- 5 ((progeni* adj3 cell*) or (stem adj3 cell*) or (precursor adj3 cell*)).ti,ab.
- 6 stem cells/or adult stem cells/or induced pluripotent stem cells/or mesenchymal stem cells/or multipotent stem cells/or pluripotent stem cells/or totipotent stem cells/
- 7 stem cell transplantation/or mesenchymal stem cell transplantation/
- 8 5 or 6 or 7
- 9 (adipo* or fat*).ti,ab.
- 10 adipose tissue/or adipose tissue, white/or abdominal fat/or intra-abdominal fat/or subcutaneous fat, abdominal/or subcutaneous fat/
- 11 adipocytes/or adipocytes, white/
- 12 Adipogenesis/
- 13 9 or 10 or 11 or 12
- 14 8 and 13
- 15 1 or 2 or 3 or 4 or 14
- 16 (cell assisted lipotransfer or cell assisted lipo-transfer or CAL).ti,ab.
- 17 (autolog* adj5 fat*).ti,ab.
- 18 ((fat* adj5 transfer*) or (fat* adj5 transplant*)).ti,ab.
- 19 Lipectomy/
- 20 Suction/
- 21 (lipo* or fat* or lipect* or adipo*).mp.
- 22 20 and 21
- 23 „tissue and organ harvesting“/or donor selection/
- 24 21 and 23
- 25 Transplants/
- 26 Transplantation/
- 27 Transplantation, Autologous/
- 28 Tissue Transplantation/ or Cell Transplantation/
- 29 (graft* or autograft* or transplant* or autotransplant*).ti,ab.
- 30 21 and (25 or 26 or 27 or 28 or 29)
- 31 tissue donors/or living donors/
- 32 21 and 31
- 33 (10 or 11) and (20 or 23 or 25 or 26 or 27 or 28 or 29 or 31)
- 34 exp Adipose Tissue/tr [Transplantation]
- 35 exp Adipocytes/tr [Transplantation]
- 36 16 or 17 or 18 or 19 or 22 or 24 or 30 or 32 or 33 or 34 or 35
- 37 15 and 36
- 38 8 and 36
- 39 37 or 38
- 40 Regenerative Medicine/
- 41 Surgery, Plastic/
- 42 exp Reconstructive Surgical Procedures/
- 43 Cosmetic Techniques/
- 44 exp Breast/
- 45 exp Breast/su, tr [Surgery, Transplantation]
- 46 mammaplasty/ or breast implantation/
- 47 Breast Implants/
- 48 Face/
- 49 Face/su [Surgery]
- 50 Rhytidoplasty/
- 51 Rejuvenation/
- 52 Blepharoplasty/
- 53 Regeneration/
- 54 Neovascularization, Physiologic/
- 55 postoperative complications/or pain, postoperative/
- 56 Calcification, Physiologic/
- 57 exp Breast Diseases/
- 58 neoplastic processes/or anaplasia/or cell transformation, neoplastic/ or neoplasm recurrence, local/or neoplasm, residual/
- 59 exp Carcinoma/
- 60 genes, brca1/or genes, brca2/
- 61 brca1 protein/or brca2 protein/
- 62 Genetic Predisposition to Disease/
- 63 exp Facial Neoplasms/
- 64 Cysts/
- 65 or/40–64
- 66 39 and 65
- 67 (breast adj6 (cancer* or tumor* or neoplas* or carcino* or adenocarcino* or malign*)).ti,ab.
- 68 ((mammary or mammary*) adj6 (cancer* or tumor* or neoplas* or carcino* or adenocarcino* or malign*)).ti,ab.
- 69 (calcificat* or cyst* or brca* or fibros* or scar* or mammograph*).ti,ab.
- 70 (plastic or reconstruct* or mamm*1plast* or mamm* plast* or facelift* or face lift* or augment*).ti,ab.
- 71 (rhytidoplast* or implant* or rejuvenat* or blepharoplast* or neovasc* or neo-vasc* or angiogen*).ti,ab.
- 72 (rhytidoplast* or (implant* and breast) or rejuvenat* or blepharoplast* or neovasc* or neo-vasc* or angiogen*).ti,ab.
- 73 vasculari*.ti,ab.
- 74 Cell Survival/
- 75 Cell Death/
- 76 Apoptosis/
- 77 Necrosis/
- 78 cell survival, cell viability, necrosis, apoptosis.ti,ab.
- 79 or/67–78
- 80 65 or 79
- 81 39 and 80
- 82 remove duplicates from 81